AHRQ Healthcare Horizon Scanning System – Potential High-Impact Interventions Report

Priority Area 01: Arthritis and Nontraumatic Joint Disease

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Statement of Funding and Purpose

This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. HHSA290201000006C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

This report's content should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual topic profiles are developed for technologies and programs that appear to be close to diffusion into practice in the United States. Those reports are sent to various experts with clinical, health systems, health administration, and/or research backgrounds for comment and opinions about potential for impact. The comments and opinions received are then considered and synthesized by ECRI Institute to identify interventions that experts deemed, through the comment process, to have potential for high impact. Please see the methods section for more details about this process. This report is produced twice annually and topics included may change depending on expert comments received on interventions issued for comment during the preceding 6 months.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in horizon scanning, assessing the leads for topics, or providing opinions regarding potential impact of interventions.

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None of the individuals compiling this information has any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor emerging technologies and innovations in health care and to create an inventory of interventions that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It will also be a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research will be able to use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption, except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the Institute of Medicine and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is identifying and monitoring new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is analyzing the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. It is NOT the goal of the AHRQ Healthcare Horizon Scanning System to make predictions on the future use and costs of any health care technology. Rather, the reports will help to inform and guide the planning and prioritization of research resources.

We welcome comments on this Potential High-Impact Interventions report. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to: effectivehealthcare@ahrq.hhs.gov.

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Background

Horizon scanning is an activity undertaken to identify technological and system innovations that could have important impacts or bring about paradigm shifts. In the health care sector, horizon scanning pertains to identification of new (and new uses of existing) pharmaceuticals, medical devices, diagnostic tests and procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, and public health and health promotion activities. In early 2010, the Agency for Healthcare Research and Quality (AHRQ) identified the need to establish a national Healthcare Horizon Scanning System to generate information to inform comparative-effectiveness research investments by AHRQ and other interested entities. AHRQ makes those investments in 14 priority areas. For purposes of horizon scanning, AHRQ's interests are broad and encompass drugs, devices, procedures, treatments, screening and diagnostics, therapeutics, surgery, programs, and care delivery innovations that address unmet needs. Thus, we refer to topics identified and tracked in the AHRQ Healthcare Horizon Scanning System generically as "interventions." The AHRQ Healthcare Horizon Scanning System implementation of a systematic horizon scanning protocol (developed between September 1 and November 30, 2010) began on December 1, 2010. The system is intended to identify interventions that purport to address an unmet need and are up to 3 years out on the horizon and then to follow them up to 2 years after initial entry into the health care system. Since that implementation, review of more than 16,200 leads about potential topics has resulted in identification and tracking of about 1,900 topics across the 14 AHRQ priority areas and 1 cross-cutting area; about 500 topics are being actively tracked in the system.

Methods

As part of the Healthcare Horizon Scanning System activity, a report on interventions deemed as having potential for high impact on some aspect of health care or the health care system (e.g., patient outcomes, utilization, infrastructure, costs) is aggregated twice a year. Topics eligible for inclusion are those interventions expected to be within 0–3 years of potential diffusion (e.g., in phase III trials or for which some preliminary efficacy data in the target population are available) in the United States or that have just begun diffusing and that have completed an expert feedback loop.

The determination of impact is made using a systematic process that involves compiling information on topics and issuing topic drafts to a small group of various experts (selected topic by topic) to gather their opinions and impressions about potential impact. Those impressions are used to determine potential impact. Information is compiled for expert comment on topics at a granular level (i.e., similar drugs in the same class are read separately), and then topics in the same class of a device, drug, or biologic are aggregated for discussion and impact assessment at a class level for this report. The process uses a topic-specific structured form with text boxes for comments and a scoring system (1 minimal to 4 high) for potential impact in seven parameters. Participants are required to respond to all parameters.

The scores and opinions are then synthesized to discern those topics deemed by experts to have potential for high impact in one or more of the parameters. Experts are drawn from an expanding database ECRI Institute maintains of approximately 350 experts nationwide who were invited and agreed to participate. The experts comprise a range of generalists and specialists in the health care sector whose experience reflects clinical practice, clinical research, health care delivery, health business, health technology assessment, or health facility administration perspectives. Each expert uses the structured form to also disclose any potential intellectual or financial conflicts of interest

(COIs). Perspectives of an expert with a COI are balanced by perspectives of experts without COIs. No more than two experts with a possible COI are considered out of a total of the seven or eight experts who are sought to provide comment for each topic. Experts are identified in the system by the perspective they bring (e.g., clinical, research, health systems, health business, health administration, health policy).

The topics included in this report had scores *and/or* supporting rationales at or above the overall average for all topics in this priority area that received comments by experts. Of key importance is that topic scores alone are not the sole criterion for inclusion—experts' rationales are the main drivers for the designation of potentially high impact. We then associated topics that emerged as having potentially high impact with a further subcategorization of "lower," "moderate," or "higher" within the high-impact-potential range. As the Healthcare Horizon Scanning System grows in number of topics on which expert opinions are received and as the development status of the interventions changes, the list of topics designated as having potentially high impact is expected to change over time. This report is being generated twice a year.

For additional details on methods, please refer to the full AHRQ Healthcare Horizon Scanning System Protocol and Operations Manual published on AHRQ's Effective Health Care Web site.

Results

The table below lists the four topics for which (1) at least preliminary phase III data were available; (2) information was compiled before October 27, 2013, in this priority area; and (3) we received six to eight sets of comments from experts between April 9, 2012, and October 29, 2013. (Seventeen topics in this priority area were being tracked in the system as of October 29, 2013.) Three topics emerged as having potential for high impact on the basis of experts' comments and their assessment of potential impact. These topics are noted by an asterisk in the table below. The material in this Executive Summary and report is organized alphabetically by disease and then intervention. Readers are encouraged to read the detailed information on each intervention that follows the Executive Summary.

Priority Area 01: Arthritis and Nontraumatic Joint Disease

Topic	High-Impact Potential
1. * Artificial cervical disc (Mobi-C) for treatment of 2-level degenerative disc disease	Moderately high
2. * Autologous mesenchymal stem cell therapy for osteoarthritis	Moderately high
3. * Autologous platelet-rich plasma therapy for osteoarthritis	Moderately high
4. Ustekinumab (Stelara) for treatment of psoriatic arthritis	No high-impact potential at this time

Discussion

The topics that emerged as higher impact were in disease categories of two-level degenerative disc disease (DDD) and osteoarthritis (OA), conditions in which experts perceived considerable unmet need because of a lack of effective treatments and the negative impact of OA on quality of life.

Cervical Degenerative Disc Disease

Cervical DDD occurs as part of the normal aging process and affects an estimated two-thirds of people aged 40 years or older in their lifetimes. Cervical DDD occurs when progressive changes in the cervical vertebral discs lead to loss of disc height, loss of water content, loss of shock-absorbing

capacity, and formation of bone spurs. Poor nutrition, smoking, atherosclerosis, type and amount of physical activity, and genetics may also contribute to DDD development. DDD of the cervical spine can result in clinical manifestations including axial neck pain, radiculopathy, myelopathy, or a combination of these conditions. Symptoms can include numbness, pain, or loss of function (e.g., gait issues, grip weakness, bowel and bladder complaints). Cervical DDD is diagnosed with a magnetic resonance imaging (MRI) scan; however, diagnosis must also include history of signs and symptoms and a physical examination. Treatments typically involve pain management, such as oral medication, epidural injections, and trigger-point injections; some patients seek osteopathic manipulation, transcutaneous electrical stimulation, and physical therapy. When these therapies fail to achieve relief, surgical treatments may be proposed, such as arthroplasty and anterior and posterior decompression and fusion.

An important and limiting complication of cervical spine fusion surgery is the potential for developing DDD in adjacent discs after surgery. Cervical artificial intervertebral disc arthroplasty is purported to relieve DDD symptoms, preserve range of motion, and prevent development of DDD at adjacent discs. However, according to Walsh as reported at the 2009 California Technology Assessment Forum, some patients with cervical DDD can have signs of degeneration at multiple levels at the time of diagnosis. No options had been approved by the U.S. Food and Drug Administration (FDA) for multilevel cervical disc replacement until the August 2013 approval of a device intended for two-level cervical disc arthroplasty, which emerging as having potential for high impact.

Artificial Cervical Disc (Mobi-C) for Treatment of Two-Level Degenerative Disc Disease

- **Key Facts:** The Mobi-C artificial cervical disc (LDR Holding Corp., Austin, TX) is the first artificial cervical disc approved to replace native cervical discs at two adjacent levels in patients with cervical DDD. The discs are intended to restore segmental motion and disc height. The device is a semiconstrained prosthesis with a mobile polyethylene insert, capable of sliding. The disc is situated between two chrome cobalt plates coated with a titanium plasma spray and hydroxyapatite coating. The design is intended to provide five independent degrees of freedom. The controlled mobility of the inserted disc purportedly helps restore and preserve the instantaneous axis of rotation to restore physiologic mobility of the spinal segment. In a randomized controlled trial, patients (n=330) with two-level DDD and radiculopathy or myeloradiculopathy with pain, paresthesias, or paralysis in a specific nerve root distribution (C3–C7) were treated with either Mobi-C or anterior cervical discectomy and fusion (ACDF) with allograft bone and anterior plate. Patients treated with Mobi-C were reported to have a significantly higher success rate than patients treated with ACDF at 6, 12, 18, and 24 months. Additionally, patients treated with Mobi-C were reported to improve more than patients treated with ACDF, as measured by Neck Disability Index scores and visual analog neck pain scales at each followup time (6 weeks and 3, 6, and 12 months). Patients treated with ACDF were reported to need reoperation more often than patients treated with Mobi-C; Mobi-C patients reported fewer complications and adverse events than did ACDF patients. The main mechanical complications reported with Mobi-C were radiologic adjacent syndrome and heterotrophic ossification.

  In August 2013, FDA approved Mobi-C for single-level cervical disc replacement and later that month, expanded the indication to two-level disc replacement. The indication is for cervical disc replacement in skeletally mature patients at two contiguous levels from C3 to C7 in adults with intractable radiculopathy with or without neck pain, or myelopathy due to

pathology attributed to the disc space level and at least one of the following conditions (confirmed by radiographic imaging): herniated nucleus pulposus, spondylosis, or visible loss of disc height compared with adjacent levels. Before implantation, patients are required to have tried at least 6 weeks of conservative treatment or continue to have progressive signs or symptoms despite conservative treatment.

Costs that some hospitals have been paying for the Mobi-C discs have been reported through ECRI Institute's PriceGuide database. As of December 5, 2013, this database showed a price range from $5,700 to $9,500; the average was about $6,900. These prices are roughly 20% to 35% higher than prices reported for single-level artificial disc counterparts from other manufacturers. Major third-party payer coverage policies generally cover artificial disc replacement at one level but have generally denied coverage for two-level disc replacement. However, no artificial discs were approved for two-level disease at the time most of those policies were published. United Healthcare lists Mobi-C as a covered device in its October 2013 policy on artificial disc replacement, but in a separate part of its policy, states that multilevel cervical disc replacement is not covered.

- **Key Expert Comments:** Overall, experts commenting on this intervention stated that a significant proportion of patients with cervical DDD have the disease at two levels and that ACDF can result in disc degeneration at adjacent levels. Thus, two-level cervical disc replacement with an effective implant could fulfill a significant unmet need by relieving patients' symptoms, preserving range of motion, and preventing the development of DDD at adjacent discs. Experts thought that available evidence suggests that Mobi-C appears to provide significant improvements in the clinical success rate and reduces reoperation rates, complications, and recovery times compared with ACDF at 24-month followup. If the clinical evidence for Mobi-C continues to show favorable outcomes, third-party reimbursement will be more likely, they thought, which would remove the barrier of high out-of-pocket patient costs for two-level disc replacement.
- **Potential for High Impact:** Moderately high

Osteoarthritis

OA, the most common form of arthritis, affects an estimated 27 million Americans, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases; it is expected to affect a greater proportion of the population as more people reach the age of 65 years or older. OA is a chronic condition characterized by the progressive loss of cartilage in one or more joints. As the cartilage that cushions a joint gradually wears away from use, bones rub against each other, causing pain, stiffness, and loss of joint flexibility. Increasing age, obesity, injury to or overuse of a joint, and genetics can all contribute to the disease. Current treatments for OA include over-the-counter pain medication, exercise and/or physical therapy, and weight loss if indicated. More severe cases may warrant injections with corticosteroids. However these agents have no anabolic or anticatabolic activity on chondrocytes, which are the cells responsible for maintaining cartilage. Two interventions were deemed by experts commenting on them to have potential to disrupt the current OA treatment paradigm because of their purported potential to regenerate articular cartilage or inhibit degenerative processes. These interventions are available both as proprietary autologous products and as autologous biologic products prepared onsite by health care facilities delivering the treatment to patients.

Autologous Mesenchymal Stem Cell Therapy for Osteoarthritis

- **Key Facts:** Autologous mesenchymal stem cell (MSC) therapy for OA consists of adult stem cells derived from the patient's own bone marrow, synovium, periosteum, skeletal muscle, or adipose tissue, and manipulated in any number of ways, including both concentrating and culturing the cells to increase their numbers and combining with growth factors and/or platelet-rich plasma (PRP) and fat matrix. Depending on the amount of processing performed, the preparation is reinjected into the patient's intra-articular space either the same day (for preparations that undergo only centrifugation with no additives) or up to a few weeks later (for highly processed, cultured preparations with additives). The methods used to prepare MSCs have not yet been standardized and differ among facilities making and administering the preparations. This may lead to different outcomes among treatment centers.
  MSCs purportedly regenerate cartilage because they secrete growth factors that differentiate into chondrocytes. The exact mechanism remains unknown. MSCs purportedly have immunomodulatory, anti-apoptotic, proliferative, and angiogenic effects on cells in the intra-articular space. Preliminary evidence suggests that intra-articular injection with some MSC preparations may reduce pain and improve function in some patients and may show improvement on radiologic endpoints, but study results are mixed at this time and controlled trials with standardized MSC preparation methods are needed to determine their true efficacy. The therapy can conceivably be made and delivered by any suitably equipped health care center, and dozens of orthopedic centers that treat OA have begun to offer it, although FDA requires an investigational new drug application and trials for any autologous cell products that are more than "minimally processed." No company has an FDA-approved autologous MSC product at this point, although one company in Texas has stated intentions to pursue FDA approval. Another company, in Colorado, had offered a cultured, highly processed autologous MSC product, but was ordered by FDA to stop; the company subsequently moved its operations for that product offshore and now offers a "minimally" processed product at its U.S. centers. Reported costs for the procedure are about $10,000. Our searches of 11 representative, private, third-party payers that publish their coverage policies online showed that all of the payers listing policies for MSCs for OA consider the therapy investigational at this time and do not cover it.
- **Key Expert Comments:** Experts stated that effective, minimally invasive OA therapies that can prevent or delay joint-replacement surgery are needed. Autologous MSC therapy has potential to be a first-line OA-treatment option if it is shown to reduce pain and regenerate articular cartilage. However, experts were cautious in their optimism about the potential impact of autologous MSC therapy because of the paucity of data demonstrating its ability to relieve symptoms and regenerate cartilage. Diffusion will be tempered by the high out-of-pocket patient costs at this time, and third-party reimbursement could be denied until evidence demonstrates a clear benefit for patients treated with clinic-prepared, minimally processed autologous MSCs.
- **Potential for High Impact:** Moderately high

Autologous Platelet-Rich Plasma Therapy for Osteoarthritis

- **Key Facts:** Autologous PRP therapy involves processing (centrifuging) the plasma portion of a patient's blood to concentrate and separate out the platelets, which are purported to secrete a wide variety of growth factors and cytokines that purportedly promote tissue

regeneration and repair. Some researchers think that because of those characteristics, PRP has potential regenerative effects on cartilage in patients with OA. PRP, collected from the patient and concentrated, is injected directly into the intra-articular space under ultrasound guidance. As with autologous MSC therapy, preparation protocols and injection frequency vary among treatment centers. The evidence base for PRP lacks sufficiently large, blinded, prospective, randomized controlled trials that compare it to other standard treatments for OA and to autologous MSCs, but it has been used by high-profile athletes trying to speed their recovery after soft-tissue injuries. Our searches of 11 representative, private, third-party payers that publish their coverage policies online found 8 payers that have specific policies denying coverage for the procedure because they consider PRP injections to be experimental or investigational. The cost of PRP therapy has been reported to range from $500 to $1,500 per injection, appearing to be less costly than autologous MSC therapy. Sometimes the two are used together. A patient may choose to receive more than one injection over time.

- **Key Expert Comments:** Overall, experts were divided on the impact that PRP might have on OA treatment. Similar to the experts' comments on autologous MSC therapy, several experts stated that if PRP were to be proved effective and become accepted first-line therapy that could regenerate joint cartilage and restore function, it would have a major impact on patient outcomes and costs of treating OA. However, more data and clinical experience are needed to standardize preparation procedures and regimens and test those regimens in randomized controlled trials to determine whether the procedure regenerates cartilage better, has a more durable effect, and leads to less need for additional OA treatment for the affected joint than other, standard therapies for OA.
- **Potential for High Impact:** Moderately high

Cervical Degenerative Disc Disease Intervention

Artificial Cervical Disc (Mobi-C) for Treatment of Two-Level Degenerative Disc Disease

Unmet need: Cervical degenerative disc disease (DDD) occurs naturally as part of the aging process and may affect up to two-thirds of people aged 40 years or older in their lifetimes.[1] DDD of the cervical spine can result in clinical manifestations including axial neck pain, radiculopathy, myelopathy, or a combination of these conditions.[1] Anterior cervical discectomy and fusion (ACDF) is the gold standard for treating cervical DDD at single or multiple levels.[2] But cervical spine fusion surgery has an important and limiting complication, the potential for developing DDD in adjacent discs after surgery, and some patients with cervical DDD can have signs of degeneration at multiple levels at the time of diagnosis.[2] Cervical artificial intervertebral disc arthroplasty is purported to relieve DDD symptoms, preserve range of motion, and prevent the development of DDD at adjacent discs. The Mobi-C® cervical disc offers the first option available for cervical disc replacement at two adjacent levels.[3,4]

Intervention: The design of the Mobi-C cervical disc is intended to restore segmental motion and disc height.[5] It is a semiconstrained prosthesis with a mobile polyethylene insert, capable of sliding, and is situated between two chrome cobalt plates coated with a titanium plasma spray and hydroxyapatite coating.[5,6] Mobi-C can be used in both one- and two-level cervical intervertebral disc replacement.[5] The design purportedly allows five independent degrees of freedom, two translational and three rotational.[6] The controlled mobility of the insert purportedly helps restore and preserve the instantaneous axis of rotation and physiologic mobility of the spinal segment.[5] Whereas fixation for cervical discs commonly uses keels or screws, Mobi-C's fixation is intended to accomplish the following:

- Eliminate the need for more-invasive fixation mechanisms by minimizing stresses between the implant and bone via the device's mobile core[7]
- Eliminate the need for invasive vertebral anchorage
- Preserve vertebral endplate integrity[4]

The device's lateral teeth have an inclined shape that purportedly facilitates insertion of the device and provides secure anchoring to the peripheral vertebral plate.[4] The device is delivered in sterile packaging and assembled and maintained between two Plug & Fit®, one-time use, radiotransparent clamps, which are used for proper device placement.[4] The patient is placed in the supine position under general anesthesia and an image intensifier is placed under the operative drapes for the duration of surgery. The surgeon makes an incision in a skin fold of the neck over the anterior edge of the sternocleidomastoid muscle if only one level is required. A vertical incision is used if two or more disc replacements are required. When the anterior column is attained, the longus colli muscles are carefully dissected.[4] Radiotransparent retractors are placed under the two longus colli muscles and the surgeon performs an anterior discectomy and replacement.[4]

Clinical trials: In a randomized controlled trial, patients (n=330) with two-level DDD and radiculopathy or myeloradiculopathy with pain, paresthesias, or paralysis in a specific nerve root distribution (C3–C7) were treated with either Mobi-C (n=225) or ACDF (n=105) with allograft bone and anterior plate. The success rate for patients treated with Mobi-C was reported as 69.7% compared with 37.4% for ACDF at 24-month followup ($p<0.0001$).[8] The authors reported that, "on average, patients in both groups showed significant improvements in NDI [neck disability index] score, VAS [visual analog scale] neck pain, and VAS arm pain from pre-operative baseline to each time point. However, the TDR [total disc replacement] patients experienced significantly greater improvement than ACDF patients in NDI score at all timepoints and significantly greater

improvement in VAS neck pain score at 6 weeks, and at 3, 6, and 12 months postoperatively. On average, patients in the TDR group also maintained preoperative segmental range of motion at both treated segments immediately postoperatively and throughout the study period of 24 months."[8]

Patients treated with ACDF required reoperation more frequently (11.4%) than patients treated with Mobi-C (3.1%; $p<0.05$).[8,9] The incidence of patients experiencing at least one serious adverse event through 24 months was 23.9% and 32.4% for Mobi-C and ACDF, respectively. Patients in the Mobi-C group had a lower rate of device-related adverse events (16.7%) than did patients treated with ACDF (34.3%).[8] The incidence rates for serious adverse events in the cervical spine definitely or possibly related to Mobi-C and ACDF were 3.4% and 14.3%, respectively. Overall, 3.6% of patients treated with Mobi-C and 6.7% of patients treated with ACDF had major complications associated with an adverse event.[8] At 48 months followup, the secondary surgery rate at the index level was 3.8% for patients treated with Mobi-C compared with 14.3% of patients treated with ACDF.[10]

The main mechanical complications reported with Mobi-C included radiologic adjacent syndrome and heterotrophic ossification; class III events were reported as permitting residual movement.[6,11]

Manufacturer and regulatory status: LDR Holding Corp., of Austin, TX, developed the Mobi-C cervical artificial disc. In March 2011, LDR submitted a premarket approval (PMA) application to FDA for Mobi-C for two-level cervical disc replacement.[12] FDA initially approved Mobi-C for single-level cervical disc replacement in August 2013.[13] Later the same month, FDA expanded approval to cervical disc replacement in skeletally mature patients at two contiguous levels from C3 to C7.[3,14] With that approval, Mobi-C became the first cervical disc replacement device to be available for two-level disc replacement during the same surgical procedure.[3] Mobi-C is indicated to treat intractable radiculopathy with or without neck pain. It is also indicated to treat myelopathy due to pathology attributed to the disc space level and at least one of the following conditions confirmed by radiographic imaging: herniated nucleus pulposus, spondylosis, or visible loss of disc height compared with adjacent levels. Before device implantation, patients must have tried at least 6 weeks of conservative treatment or must have continuing, progressive signs or symptoms despite conservative treatment.[14]

Diffusion: Costs that some hospitals have been paying for the Mobi-C discs have been reported to ECRI Institute's PriceGuide database. As of December 5, 2013, this database showed the range of prices paid to be from $5,700 to $9,500; the average was about $6,900. These prices are roughly 20% to 35% higher than prices reported for single-level artificial disc counterparts from other manufacturers.[15] Although the upfront costs of cervical disc replacement may be higher than for ACDF, these initial costs could be offset by reductions in the numbers of patients requiring revision surgery after ACDF or in reduced rates of damage to adjacent discs.

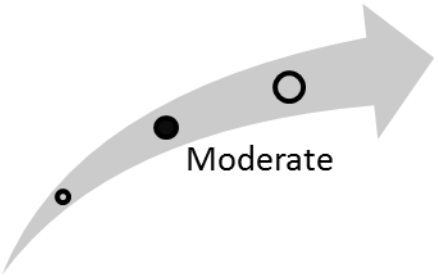
Our searches of 11 representative, private, third-party payers that publish their coverage policies online (i.e., Aetna, Anthem, Blue Cross/Blue Shield Alabama, Blue Cross/Blue Shield Massachusetts, CIGNA, HealthPartners, Humana, Medica, Regence, United Healthcare, Wellmark) found 7 have policies that deny coverage because they consider multilevel cervical disc replacement investigational.[16-21] The United Healthcare policy lists Mobi-C as a covered device in one part of its policy, but separately states in the policy that multilevel cervical disc replacement is not covered.

Clinical Pathway at Point of This Intervention

Common cervical DDD treatments include medications, osteopathic manipulations, epidural injections, trigger-point injections, transcutaneous electrical stimulation, and physical therapy. Because smoking has been shown to inhibit spinal healing, physicians also encourage smokers in

this population to quit.[22] Surgical treatments are rare, but may be required to help control symptoms and allow a patient to function fully;[22] they include arthroplasty, anterior and posterior decompression, and fusion surgery.[1]

Figure 1. Overall high impact potential: Artificial Cervical Disc (Mobi-C) for treatment of two-level degenerative disc disease



Overall, experts commenting on this intervention stated that a significant proportion of patients have two-level DDD and that ACDF can degenerate discs at adjacent levels. Thus, two-level Mobi-C Cervical Disc replacement could fulfill a significant unmet need by relieving symptoms, preserving range of motion, and preventing deterioration at adjacent discs. Experts thought that available evidence suggests that Mobi-C may improve clinical success rates and reduce reoperation rates, complications, and recovery times compared with ACDF outcomes. If the clinical evidence for Mobi-C continues to show favorable outcomes, third-party payment, which is lacking now, might follow. This lack of payer coverage appears to be the largest barrier to acceptance and diffusion because of high out-of-pocket costs that patients would otherwise incur. If Mobi-C is shown to improve outcomes enough to benefit patients and reduce the need to reoperate for adjacent DDD after fusion, two-level disc replacement could gain wider acceptance. Based on this input, our overall assessment is that this intervention is in the moderate high-impact-potential range.

Results and Discussion of Comments

Six experts, with clinical, research, and health systems backgrounds, offered perspectives on this intervention.[23-28] We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: Multilevel DDD presents a significant unmet need for new treatment options because ACDF can lead to degeneration at discs above and below the operation site, the experts stated. Complications from ACDF often require additional surgery, one clinical expert noted. Two-level cervical disc replacement with Mobi-C appears to provide a lower rate of complications and reoperations compared with ACDF treatment, experts noted. Two-level disc replacement was also reported as providing improved range of motion, which might reduce complications and future operations, one clinician stated. However, the experts stated more studies comparing Mobi-C with ACDF are needed to confirm these preliminary results.

Acceptance and adoption: Clinicians are generally expected to accept the procedure if the evidence continues to demonstrate superior efficacy and mobility with fewer complications than ACDF, the experts thought. However, some clinicians may be reluctant to put time into learning a new technique if they think ACDF provides successful treatment most of the time, one research expert stated. Patients are expected to be hesitant about any cervical spine surgery, because of the risk of complications to spinal nerves, one clinical expert stated. Lack of reimbursement and the classification of multilevel disc replacement as investigational by third-party payers may present a significant barrier to acceptance and diffusion for both patients and clinicians. Additional clinical

evidence of improved outcomes and reduced costs of care could increase acceptance by payers and, ultimately, patients and clinicians.

According to some experts, increased training and time required for more complicated surgical procedures are expected to increase the cost of care. However, these costs could be offset by improved surgical outcomes, reduced complications, shorter hospital stays, a shorter course of physical therapy, and reduced need for revision surgery. Those factors might increase payer acceptance, thought one clinical expert.

Health care delivery infrastructure and patient management: Offering Mobi-C at surgical centers would require additional training for physicians and staff, the experts stated. Additionally, surgical procedures are expected require more time, increasing demands on surgical suites that offer the procedure. However, these demands could be offset by the many of same factors that could reduce costs—improved surgical outcomes, reduced complications, shorter hospital stays, and a lower rate of additional surgeries required, the experts stated.

Health disparities: Mobi-C could increase health disparities, according to expert comments. The experts thought that the complexity of the procedure would limit diffusion to specialty centers and further, that the current lack of reimbursement for two-level cervical disc replacement surgery and the total out-of-pocket cost of surgery indicate that only wealthy patients would be expected to receive treatment with this procedure until widespread acceptance and coverage from public and private payers occurs.

Osteoarthritis Interventions

Autologous Mesenchymal Stem Cell Therapy for Osteoarthritis

Intervention: Mesenchymal stem cells (MSCs) are adult stem cells that are involved in maintaining the relative stability of internal physiologic conditions of many tissue types in the body.[29] As progenitor cells, MSCs are purported to retain the ability to differentiate into a number of cell types, including chondrocytes, which are the cells responsible for maintaining cartilage.[30,31] Autologous MSCs are derived from the patient and can be isolated, concentrated, cultured, and expanded in vitro and returned to the patient with the intention of treating the large cartilage defects observed in osteoarthritis (OA). However, the mechanism by which these cells lead to cartilage generation is still unclear.[29] MSCs may differentiate into chondrocytes and fill in a cartilage defect. Additionally, MSCs are known to have effects on the intra-articular environment, including immunomodulation, host cell survival, endogenous tissue progenitor cell proliferation, local angiogenesis, and fibrosis inhibition.[29]

The methods used to prepare autologous MSCs have not yet been standardized; the cells can be isolated from bone marrow, synovium, periosteum, skeletal muscle, or adipose tissue.[30] MSCs isolated from these different tissues purportedly exhibit differences in their ability to proliferate and their propensity to differentiate into chondrocytes.[30] To have an adequate number of MSCs for treatment, the cells from a tissue sample must be concentrated by centrifugation and/or expanded in vitro through the culture and addition of growth factors, sometimes including platelets.[31,32] The method chosen to acquire cells may also influence the nature of the MSCs used for treatment. Additionally, patient characteristics such as age and the presence of OA have been shown to affect the ability of autologous MSCs to differentiate into chondrocytes.[30,33] Thus, many factors can introduce variability in this procedure. Autologous MSCs have also been given with other therapies, including platelet-rich plasma (PRP) therapy.

Clinical trials: Many case series have been published, but no definitive, well-designed, controlled trials using standardized methods of preparation are available yet.

Results reported from a patient registry (n=184) of a proprietary MSC procedure (Regenexx-SD™) stated 91% of patients (n=35 reporting at 18 months; a 58% reporting rate) with knee OA treated with MSC self-reported symptom improvement from baseline. Mean symptom improvement was 50% or more 18 months after treatment.[34]

In one trial, patients (n=18) who received intra-articular injections of adipose-derived autologous MSC combined with PRP, after arthroscopic débridement, for treating knee OA experienced the following:[35]

- A significant decrease in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores from 49.9 points at baseline to 30.3 points at the mean followup of 24.3 months ($p<0.001$)
- Improvement in Lysholm scores from a mean baseline value of 40.1 points to 73.4 points at the last followup ($p<0.001$)
- Improvements in mean VAS score from 4.8 at baseline to 2.0 at the last followup ($p=0.005$)
- Improvement in the whole-organ magnetic resonance imaging (MRI) score from 60.0 points at baseline to 48.3 points at the last followup ($p<0.001$) (clinical significance uncertain)
- Improvement in the cartilage whole-organ MRI score from 28.3 points at baseline to 21.7 points at the last followup ($p<0.001$) (clinical significance uncertain)

Improvements in clinical and MRI results were purported to be positively related to the number of stem cells injected.[35]

In patients with knee OA and a Kellgren-Lawrence status of 2, 3, or 4 (n=23) who were treated with a combination of autologous MSC (concentrated bone marrow isolate), PRP, and fat matrix injected into the intra-articular space, improvements in several disease measures were reported for patients at 6-month (n=12) and 12-month (n=10) followup. The investigators reported that patients treated with MSC therapy had the following:[32]

- Improvements from baseline in patient pain, measured on a VAS, of 34% and 25% at 6 and 12 months, respectively
- Improvements in patient global assessment of disease of 33% and 33% from baseline at 6 and 12 months, respectively
- Improvements in physician global assessment of 51% and 53% from baseline at 6 and 12 months, respectively
- Improvements in 50-foot walk pain of 26% and 17% from baseline at 6 and 12 months, respectively
- Improvements in WOMAC scores of 20% and 8% from baseline at 6 and 12 months, respectively
- Mean improvements of patellofemoral cartilage thickness at seven standardized points of 0.4 mm and 0.8 mm from baseline to 6 months and 12 months, respectively.[32]

Manufacturer and regulatory status: FDA categorizes therapeutic stem cell–based products as human cells, tissues, and cellular and tissue-based products (HCT/Ps), which it defines as "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient."[36]

Whether an HCT/P is subject to FDA regulation as a biological product, drug, or device depends on how much it has been manipulated after collection. These products are regulated under the authority of both the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act (FDCA).[37] FDA contends that most of the autologous MSCs used for OA "are highly processed, are used for other than their normal function, are combined with non-tissue components, or are used for metabolic purposes" and are subject to regulation.[36,37] Thus, they are subject to requirements for filing as an investigational new drug (IND), investigational device exemption (IDE), or new biologic, depending on how FDA categorizes the product and which division has product oversight. Considerations addressed in FDA's decision to regulate HCT/Ps include the following:[38]

- Has the product been more-than-minimally manipulated (i.e., processing has altered the biological characteristics)?
- Is the product intended for homologous function?
- Has the product been combined with any nontissue or noncellular components?
- Does the product's overall effect on the physiology depend on the body's metabolism?

In 2010, FDA filed an injunction against manufacturer Regenerative Sciences, Inc., of Broomfield, CO, asserting that its stem cell products were considered drugs according to the FDCA and biological products under the Public Health Service Act. FDA asserted that the company was manufacturing these agents without its approval, without following good manufacturing practice, and without proving the treatment's safety and efficacy.[39] The company contended that its autologous MSC therapy represented a "practice of medicine" under Colorado state law, and so was not subject to FDA oversight.[40,41] On July 23, 2012, the U.S. District Court for the District of Columbia ruled that the company's ex vivo expansion and manipulation of autologous MSCs exceeded minimal processing and, thus, was subject to FDA regulatory oversight.[42] The court also stated that the presence of the antibiotic doxycycline (which had been shipped in interstate commerce and was added to the cell culture) made the cell product subject to regulation under the

FDCA and the Public Health Service Act.[40] The court granted FDA a permanent injunction against Regenerative Sciences for use of Regenexx™ MSCs unless the company completes the required FDA regulatory approval processes.[40]

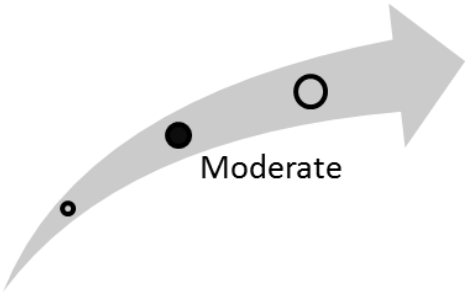
The company continues to offer a modified Regenexx procedure, which it states consists of MSCs derived from bone marrow aspirate and venous blood that are collected, processed, and injected the same day (Regenexx-SD).[43] The manufacturer states that the new Regenexx procedure offered in the United States is compliant with Code of Federal Regulations 21 Part 1271, which sets forth HCT/P regulations,[44] falling under part 1271.15 (b), which exempts establishments that remove HCT/Ps from an individual and implant them into the same individual during the same surgical procedure.[45,46] At least 18 medical facilities in the US offer the Regenexx procedure.[47]

Diffusion: Although the efficacy of autologous MSCs treating OA has not yet been established, the treatment could conceivably be performed at any suitably equipped health care center, and some physicians have begun to offer it as a treatment.[48,49] One center offering MSC therapy quoted a price of about $10,000 for a regimen that involves a single injection of a bone marrow concentrate, PRP, and autologous fat scaffold plus the required pretreatment and posttreatment assessments.[50,51] Our searches of 11 representative, private, third-party payers that publish their coverage policies online (i.e., Aetna, Anthem, Blue Cross/Blue Shield Alabama, Blue Cross/Blue Shield Massachusetts, CIGNA, HealthPartners, Humana, Medica, Regence, United Healthcare, Wellmark) found that 5 deny coverage for MSC therapy for OA, stating that MSC therapy is investigational because of insufficient evidence or insufficient long-term safety or efficacy outcomes.[52-56]

Clinical Pathway at Point of This Intervention

Patients with OA are often prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, nabumetone, and naproxen as well as the COX-2 inhibitor celecoxib. Physicians can recommend exercise, physical and/or occupational therapy, and weight loss. More severe cases of OA may warrant using prescription painkillers, corticosteroid injections, or viscosupplementation. For patients with severe, persistent symptoms despite optimal treatment, clinicians can recommend surgery, including joint replacement.[57] MSC therapy is intended to be used as a cartilage-restoring technique in patients with uncontrolled OA pain whose disease is not responding to conservative therapy and who do not want to undergo knee replacement.

Figure 2. Overall high-impact potential: autologous mesenchymal stem cell therapy for osteoarthritis



Experts commenting on this technique stated that effective, minimally invasive OA therapies that can prevent or delay joint-replacement surgery are needed. Autologous MSCs have the potential to be the first treatment for OA that could regenerate articular cartilage and could provide additional benefit compared with PRP therapy. However, data are limited regarding the ability of autologous MSCs to improve OA symptoms and regenerate cartilage, and experts were cautious in their assessment of MSC therapy's potential impact. Additionally, the current lack of third-party

payer coverage and high out-of-pocket costs for patients are expected to temper the impact of autologous MSC therapy for OA until more evidence accumulates to demonstrate its clinical benefit. Based on this input, our overall assessment is that this intervention is in the moderate high-impact-potential range.

Results and Discussion of Comments

Six experts with clinical, research, health systems, and health administration backgrounds, offered perspectives on this intervention.[58-63] We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: Current OA therapies treat only the symptoms and do not restore cartilage or joint function, the experts stated; thus, a significant unmet need exists for treatments that can restore cartilage and obviate or delay the need for joint replacement.

In terms of health outcomes, preliminary data were encouraging, the experts said, and they were cautiously optimistic about the potential of MSCs to improve patient health outcomes. They thought MSCs could potentially relieve symptoms and regenerate cartilage, providing a novel treatment option to reverse the disease course of OA and reducing the need for additional therapies. Patients who are physically inactive due to OA or who were physically inactive and developed OA could be motivated to adopt a more active lifestyle if MSC can effectively relieve their symptoms, improving health outcomes, one research expert noted.

Acceptance and adoption: The current evidence would not convince most clinicians that the procedure is effective, noted one expert representing a research perspective. However, the experts opined that more clinicians would accept MSC therapy if the procedure were to be found safe and effective in larger, randomized controlled trials, because MSC therapy is less invasive than joint-replacement surgery. However, one expert representing a clinical perspective stated that some clinicians are very skeptical of any biologic therapy in general. Additionally, two experts representing a research perspective theorized that concern regarding the development of cancerous growths could limit clinician acceptance. One expert representing health systems perspective noted that additional training for the procedure and lack of third-party reimbursement could be barriers to clinician acceptance.

Patients with OA have a great need for effective treatment and some patients are currently paying out of pocket for treatments such as PRP, thus patient acceptance would likely be high, noted one clinical expert. Additionally, the advantages compared with conservative treatment are considerable, and the reported adverse events appear minimal, which could lead to high patient acceptance, one health systems expert opined. The largest barrier to patient acceptance would be reimbursement, noted two health systems experts. Experts identified additional barriers to patient acceptance including procedural difficulties in obtaining tissue for MSC therapy (i.e., bone marrow harvest) and potential for developing malignancies.

MSC could be the first treatment option for OA that could regenerate cartilage; however, data are limited. Thus, experts were cautiously optimistic about the potential impact of MSC therapy while the evidence base increases.

Health care delivery infrastructure and patient management: Changes in infrastructure, such as buying equipment and creating facilities to handle and isolate MSCs in an FDA-compliant manner, will be needed in many locations where there may already be demand for the procedure, even though MSC injection is similar to other injections used to treat OA, the experts stated.

The experts stated that MSC therapy could reduce the cost of care if the procedure can reduce or delay the need for joint-replacement surgery. According to one health systems expert, patients with OA spend about $2,600 in out-of-pocket costs annually to manage their symptoms; thus, a treatment

that restores cartilage could have a significant financial impact compared with the cost of long-term conservative symptom management. However, another expert representing a research perspective stated the average cost of joint replacement therapy is about $16,000, which could be less than the total cost of MSC therapy, depending on the number of treatments required.

In terms of patient management, experts were divided on the role MSC therapy may play in treating OA. The therapy could provide a major advance in treatment for many patients if it becomes the first therapy shown to regenerate joint cartilage and restore function, stated two experts, representing research and health systems perspectives. They thought individuals using MSC therapy could avoid the cost, complications, and recovery time of joint-replacement surgery. However, one research expert added patients could have to go through a relatively invasive procedure to harvest MSCs. Taking the alternative position that MSC therapy would be minimally disruptive to patient management, one clinical expert stated that OA is already treated with intra-articular injection.

Health disparities: If the procedure is adjunctive to current therapies it could increase health disparities by adding to costs. Some experts agreed that lack of third-party payment for MSC therapy and its implementation in specialty centers are more likely to create health disparities in treating OA.

Autologous Platelet-Rich Plasma Therapy for Osteoarthritis

Intervention: PRP involves processing a plasma portion of a patient's blood to achieve a higher-than-normal concentration of platelets, which are purported to secrete a wide variety of growth factors and cytokines and may promote tissue regeneration and repair.[64] As such, PRP is thought by some investigators and clinicians to have potential to address the underlying pathology of OA rather than only ameliorating symptoms of the disease.[65] PRP has been used in a number of hemostatic applications as well as for treating soft-tissue injuries such as tendinitis and chronic wounds.[64]

In PRP, patient blood is collected and centrifuged to concentrate platelets in a small volume of plasma (about 5 mL) for each injection; clinicians inject it into the patient's intra-articular space under ultrasound guidance.[65-68] Typically, multiple injections are given over the course of several weeks.

Clinical trials: In one prospective trial, patients with bilateral early knee OA received a blinded, single intra-articular PRP injection (Group A; n=54 knees), two PRP injections 2–3 weeks apart (Group B; n=50 knees), or saline injection (Group C; n=46 knees). Followup evaluation was performed at 3 weeks, 3 months, and 6 months by a blinded, independent observer. Significant improvement in all WOMAC parameters ($p<0.05$) were noted in both PRP-injection groups beginning at about 2–3 weeks with a trend of slight symptom worsening at the 6 month followup.[69] The percentage benefit from baseline to each followup time point was greater in patients in both PRP-injection groups compared with patients in the saline-injection group ($p<0.001$). No significant difference in clinical improvement was observed between patients treated with single or dual PRP injections. Patients treated with PRP reported mild adverse events, including sweating, which occurred within 30 minutes and could be attributed to platelet dosage, nausea, and headache.[69]

In another prospective study, patients with OA were treated with one intra-articular injection of PRP or three intra-articular injections of hyaluronic acid (n=45). Patients treated with PRP had significant improvements in the Knee Injury and Osteoarthritis Outcome Score and visual pain scale at 3- and 6-month followups.[70] No severe adverse events were observed. The cost of one PRP treatment was purported to be lower than the cost of three hyaluronic acid treatments.[70]

In another trial, patients (n=120) with knee OA Kellgren and Lawrence grade 1, 2, or 3 were treated with three intra-articular injections of either PRP or hyaluronic acid. Statistically significant improvements in the WOMAC and Numeric Rating Scale scores were observed in patients who received PRP injections at 3- and 6-month followup. No severe adverse events were observed by the investigators.[71]

In a randomized, double-blind, controlled trial, patients (n=109) with knee OA Kellgren-Lawrence grade 1, 2, or 3 were treated with three weekly injections of PRP or hyaluronic acid and evaluated at 12-month followup. Both groups showed clinical improvement at followup with no statistical difference between groups. The authors reported a "trend" for improvement in the PRP group patients with low-grade articular degeneration (Kellgren-Lawrence score up to 2). No serious adverse events were reported. Mild pain and effusion after the injections were reported, more in the PRP group than in the hyaluronic acid group ($p=0.039$).[72]

In a study of patients with knee OA (n=261 patients with Outerbridge grades I–IV and symptoms of more than 3 months' duration) who were treated with three intra-articular PRP injections every 2 weeks, 6-month followup showed statistically significant improvements in the PRP group for pain, stiffness, and functional capacity ($p<0.0001$).[73] No adverse events were reported.

In another trial, patients with knee OA (n=100 patients, 115 knees) received three intra-articular PRP injections. Statistically significant improvements in all clinical scores (International Knee Documentation Committee form, EQ [EuroQol] VAS quality-of-life score) were reported between the baseline evaluation, the end of the therapy, and between baseline and 6- and 12-month followup ($p<0.0005$).

In the trial, the results declined significantly by and after 12-month followup ($p=0.02$) but were still better than at baseline ($p<0.0005$).[66] By 24-month followup, all evaluated outcomes were significantly lower than those observed at 12-month followup. Better results were obtained in younger patients ($p=0.0001$) and in patients with lesser degrees of cartilage degeneration ($p<0.0005$). The median duration of the clinical improvement provided by PRP for knee OA was 9 months.[68]

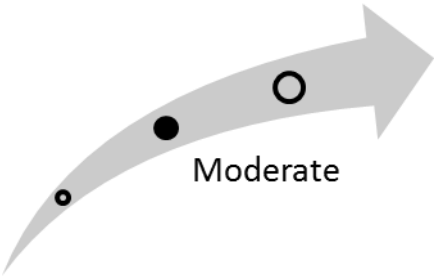
Manufacturer and regulatory status: Autologous PRP is not considered a drug or a therapeutic substance by FDA; therefore, the preparation is not subject to regulatory marketing approval. The patient undergoes apheresis to collect blood to yield the plasma that is centrifuged to concentrate platelets at a facility (such as a hospital blood bank or blood processing laboratory) according to standard blood-processing safety procedures. Thus, the treatment is readily available and may be employed by physicians.[64] Many devices have FDA marketing approval for use in preparing PRP.[66]

Diffusion: The therapy's cost reportedly is from $500 to $1,500 per injection.[74] Our searches of 11 representative, private, third-party payers that publish their coverage policies online (i.e., Aetna, Anthem, Blue Cross/Blue Shield Alabama, Blue Cross/Blue Shield Massachusetts, CIGNA, HealthPartners, Humana, Medica, Regence, United Healthcare, Wellmark) found 8 payers that have specific policies denying coverage for the procedure because they consider PRP injections to be experimental or investigational.[75-82]

Clinical Pathway at Point of This Intervention

Patients with OA are frequently prescribed NSAIDs such as aspirin, ibuprofen, nabumetone, and naproxen as well as the COX-2 inhibitor celecoxib. Physicians can recommend exercise, physical and/or occupational therapy, and weight loss. More severe cases of OA may warrant using prescription painkillers, corticosteroid injections, or viscosupplementation. For patients with severe, persistent symptoms despite optimal treatment, clinicians can recommend surgery, including joint replacement.[57] If proved effective for treating knee OA, PRP therapy would be employed as a cartilage-restoring technique in patients with uncontrolled OA pain whose disease is not responding to conservative therapy.

Figure 3. Overall high-impact potential: autologous platelet-rich plasma therapy for osteoarthritis



Overall, experts commenting on this intervention were divided on the impact that PRP might have on OA treatment. Treatment options that can restore cartilage and bridge the gap between pain relief and joint replacement are needed, and several experts stated that if PRP were to become

standard first-line therapy and actually regenerate joint cartilage and restore function, it would have a large impact on patient outcomes and be a major cost-saving advance in OA treatment. However, more data and clinical experience are needed to demonstrate whether the procedure regenerates cartilage, has a durable effect, and reduces the need for additional OA treatment for the affected joint. Based on this input, our overall assessment is that this intervention is in the moderate high-impact-potential range.

Results and Discussion of Comments

Seven experts, with clinical, research, health systems, and health administration backgrounds, offered perspectives on this intervention.[83-89] We have organized the following discussion of expert comments according to the parameters on which they commented.

Unmet need and health outcomes: Current therapies for OA treat only the symptoms and do not restore cartilage or joint function, the experts stated. Thus, a significant and growing unmet need exists for noninvasive treatments that can restore joint cartilage and function and delay or eliminate the need for joint replacement surgery.

Experts were cautiously optimistic about PRP therapy's potential to improve patient health outcomes by relieving symptoms, regenerating cartilage, and preventing or delaying joint-replacement surgery. However, some experts stated that large, randomized, double-blind controlled trials are needed to better understand PRP's effects on knee and hip OA. One health systems expert stated that data from current trials suggest that the effects of PRP might last for only 6–9 months, which suggests PRP has only moderate potential to improve health outcomes.

Acceptance and adoption: PRP may provide the most clinical benefit in younger patients, which could affect the impact and diffusion of the intervention, the experts theorized. Cost could also affect acceptance. Experts stated that the PRP-injection technique could gain broader acceptance if it is shown to be effective in well-designed controlled trials and if that results in third-party payer coverage. One clinical expert also thought that PRP costs were high for a treatment that had only subjectively reported results. However, if the procedure can eliminate the need for joint-replacement surgery in some patients, PRP injections are expected to be cost saving.

Health care delivery infrastructure and patient management: Because patients with OA already have the option of treatment delivered by injections in the knee or hip, minimal changes in infrastructure and patient management would be seen with implementing PRP, experts thought. However, changes in patient management and infrastructure might occur because of fewer joint-replacement surgeries, which would cause many inpatient procedures to be handled as outpatient procedures, reducing costs. Additionally, some equipment may need to be purchased for preparing PRP, and staff would need training in handling blood collection and preparing PRP.

Health disparities: The effect of this intervention on health disparities is unclear. Two experts with research and systems perspectives stated that the simple, minimally invasive nature of the procedure might enable easy adoption of the procedure in underserved areas. Other experts thought the lack of reimbursement currently associated with the procedure would increase health disparities if the procedure improves outcomes.

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